K003908

1 of 7

MAR - 8 2001

510(k) Summary
(As required by 21 CFR 807.92(a))

A.	Submitter Information	Bioject, Inc. 7620 SW Bridgeport Road Portland, Oregon 97224 Phone: 800-683-7221 ext. 424 Fax: 503-624-9002 Email: nancy@bioject.com Contact: Nancy J. Gertlar Director, QA/RA Date: December 15, 2000
B	Device Information Trade/Proprietary Name:	SeroJet™
	Common Name:	Needle Free Injector, Jet Injector
	Classification Name:	Jet Injector, Non-Electrically Powered Fluid Injector
	Predicate Device(s):	• Clicker™ (cool.click™) K994384
	Device Description:	SeroJet™ Needle-Free Self-Injection Device for Personal Use with Serostim® [somatropin (rDNA origin) for injection]. Needle Free Injector, Jet Injector
	Intended Use:	SeroJet™ Needle-Free Self-Injection Device for Personal Use with Serostim® [somatropin (rDNA origin) for injection].
C	Comparison of Required Technological Characteristics:	This submission changes the labeling of the Clicker™ (cool.click™) to allow the device to be used for needle-free subcutaneous administration of Serostim® [somatropin (rDNAorigin) for injection]. There are no significant changes in device design or function.

D Summary and Conclusion of Nonclinical and Clinical Tests:

GROWTH HORMONE DELIVERY USING A NEEDLE-FREE JET-INJECTOR

A number of clinical and laboratory studies were completed to prepare for an FDA submission for Serostim® to be used with a needle-free device®. These included laboratory studies designed to address the ability of Serostim® to remain intact after administration through the jet-injector and measurement of any Serostim®, which may adsorb to the plastic component parts.

LABORATORY STUDIES

The goals of the laboratory studies were to evaluate potential shearing and fragmentation of Serostim® and the interaction of growth hormone with the various plastic device components. Three protocols were completed to reach the above goals.

SHEAR STRESS TESTING

SeroJet™ utilizes a spring to induce a high-pressure injection of growth hormone through the skin. Protocol P-00048-02 was conducted to determine the effect of shear stress on Serostim®. One lot of the 6.0 mg vial Serostim® and one lot of 4.0 mg vial Serostim® were tested. Technical report R-00079-02 summarizes the results. Results were within assay variability for high-pressure liquid chromatography (HPLC) analysis, physical tests and pH. Therefore, shear stress caused by SeroJet™ did not physically alter the structure of Serostim®.

CHEMICAL COMPATIBILITY TESTING

CLEAR VIEW NOZZLE STUDY

SeroJet™ utilizes a sterile plastic Stem Tip and Clear View Nozzle to perform a high-pressure injection of growth hormone through the skin. Protocol P-00046-02 was performed to assess interaction of growth hormone with the plastic components of the needle-free jet-injector. One lot of the 6.0 mg vial Serostim® and one lot of 4.0 mg vial Serostim® were tested. Technical report R-00080-02 summarizes the results. Results were within assay variability for HPLC analysis, physical tests and pH. Therefore, the Clear View Nozzle and Stem Tip are suitable for use with Saizen®

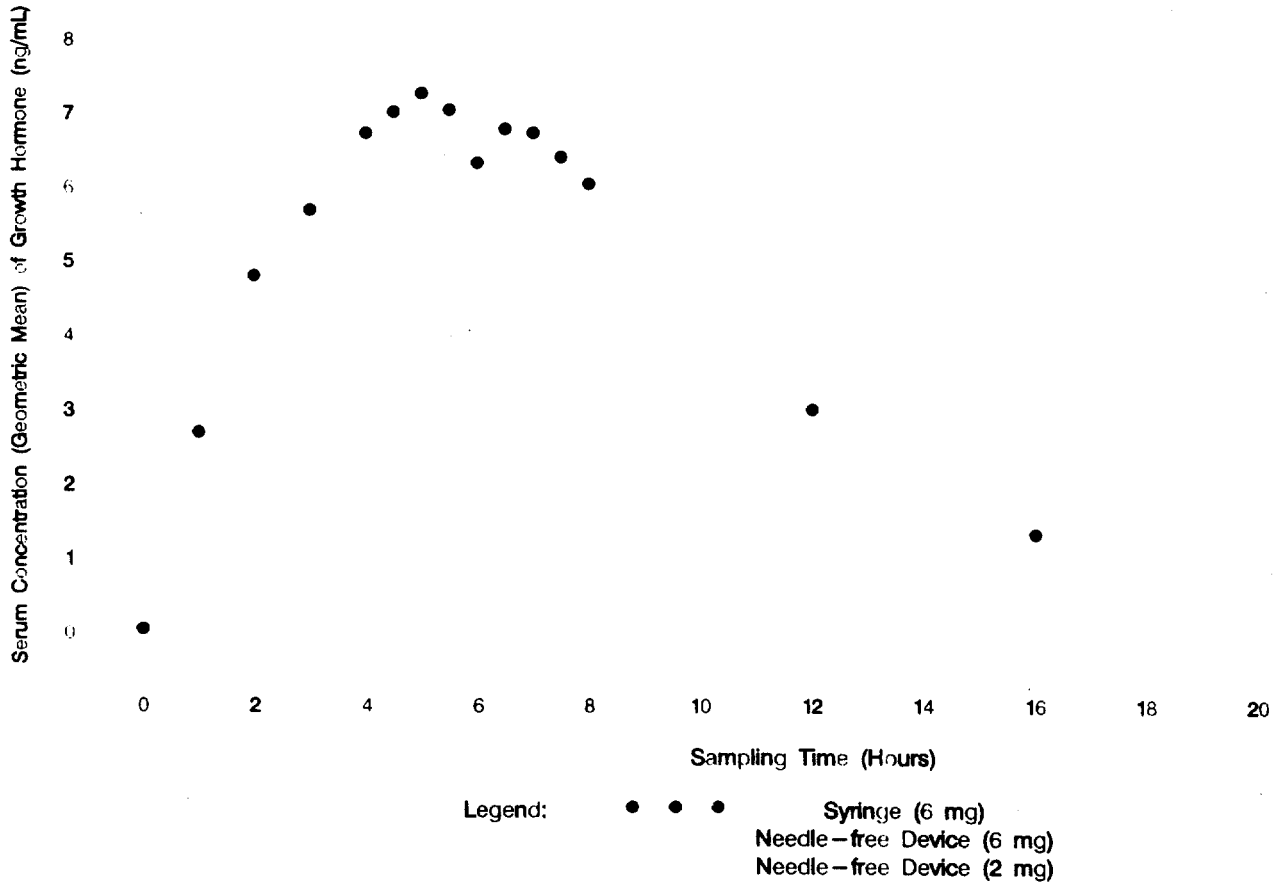
VIAL CONNECTOR STUDY

Protocol P-00047-02 examined the Vial Connector needed on the vial of growth hormone to facilitate drawing up the material into the injector. The growth hormone samples were observed at seven and fourteen days for particulates by holding up to the light, checking against black paper and checking against white paper. The samples were also tested for pH and assessed for purity by SE-HPLC. Technical report R-00078-02 summarizes these results. Results demonstrated within- assay variability for HPLC analysis, physical tests and pH. Therefore, the Vial Connector is suitable for use with Serostim®.

Biostatistical Analysis of a Randomized, Multi-Dose, Three-Way Crossover Relative Bioavailability and Dose Proportionality Study of Serostem®

A randomized, multiple–dose, three-way crossover relative bioavailability and dose proportionality study of Serostem® administered subcutaneously by syringe (6 mg in one ml.) or needle-free device (2 and 6 mg in 0.5ml) in tested normal healthy adult male and female subjects (ages 19- 48 years) was completed to determine bioequivalence between the conventional subcutaneous injection of GH and GH injected using a needle-free jet-injector. Statistical bioequivalence analyses were based on 26 subjects. In the clinical pharmacokinetic study, the measured GH levels from subjects using the needle injection and the needle-free jet-injector were similar during the entire 24 hours of blood monitoring. (Figure 1)

Figure 1



The maximum concentration of GH and the peak time for the maximum GH concentration were also not statistically different. The data for AUC, $AUC_{(t\ last)}$ and C_{max} were dose corrected and log transformed prior to analysis. The data for t_{max} and $t_{1/2}$ were assessed for adherence to assumptions. For $AUC_{t\ last}$, the 90 % confidence interval for the ratio of test to reference expressed, as a percentage was (0.81.3, 91.1) falling within the (80%, 125%) interval required for bioequivalence as specified in the protocol. For AUC, the 90 % confidence interval for the ratio of test to reference expressed as a percentage was (83.4, 94.2) also falling within the (80 %, 125 %) interval required for bioequivalence. For untransformed t_{max}, the p-values associated with the Shapiro-Wilks tests of normality were not statistically significant for intrasubject error. Analysis results for the test of dose proportionality between the Needle-free Device (2- mg) and the Needle-free Device (6-mg) was concluded on the basis of AUC (T last) 90 % confidence interval (84.0, 94.1), AUC 90 % confidence interval (82.6, 93.2) and C max 90% confidence interval (92.4, 114.5).

The serum IGF-I values measured every six hours for 24 hours after injection also were very similar when comparing both the needle 6-mg and Needle- free Device 6-mg (Figure 2). These concentrations were not dose adjusted in the analysis or presentation. No statistically significant differences were found between the 6mg needle and 6-mg needle-free treatments for all of these time points which indicates that the two treatments generated immunological responses in IGF-1 of similar magnitude. On the other hand, statistically significant differences were found between the 2- mg and the 6- mg doses of the Needle-free system at 12, 18, and 24 hours with the 6- mg treatment displaying higher concentrations for these timepoints than the 2 mg treatment.

Analog scales were developed to evaluate drug penetration of the skin, bleeding and bruising immediately after injection, thirty minutes after injection and twenty-four hours after injection. Results for the penetration rating were identical for three treatments. For all three treatments, the entire dose penetrated the skin for the 26 subjects who had non-missing data for this measurement. No formal statistical tests were performed on this rating. Three subjects in the first two periods were dropped due to wet injections resulting in a total wet injection rate after 109 injections of 2.75%.

With regard to the bleeding scores, no statistically significant differences were found between the Needle-free (6- mg) or the Needle-free (2- mg) treatments and the Syringe. The comparison between the Needle-free Device (6- mg) and the Syringe was not statistically significant (p=0.0570). Slightly more subjects experienced minimal to severe bleeding after the Needle-free (6-mg) than after the Syringe treatment.

With regard to the bruising score, the results were similar for all three treatments at all time points measured. Immediately after the injections, no subjects reported any bruising for any of the three treatments: At 2 hours after the injection, only one subject receiving the Needle-free (6- mg) treatment and 3 subjects receiving the Needle-free (2 mg) treatment reported slight bruising; at 24 hours after injection, 3 subjects receiving the Needle-free (2- mg) treatment and 2- subjects receiving the Syringe treatment reported slight bruising. No formal statistical tests were performed on the bruising scores.

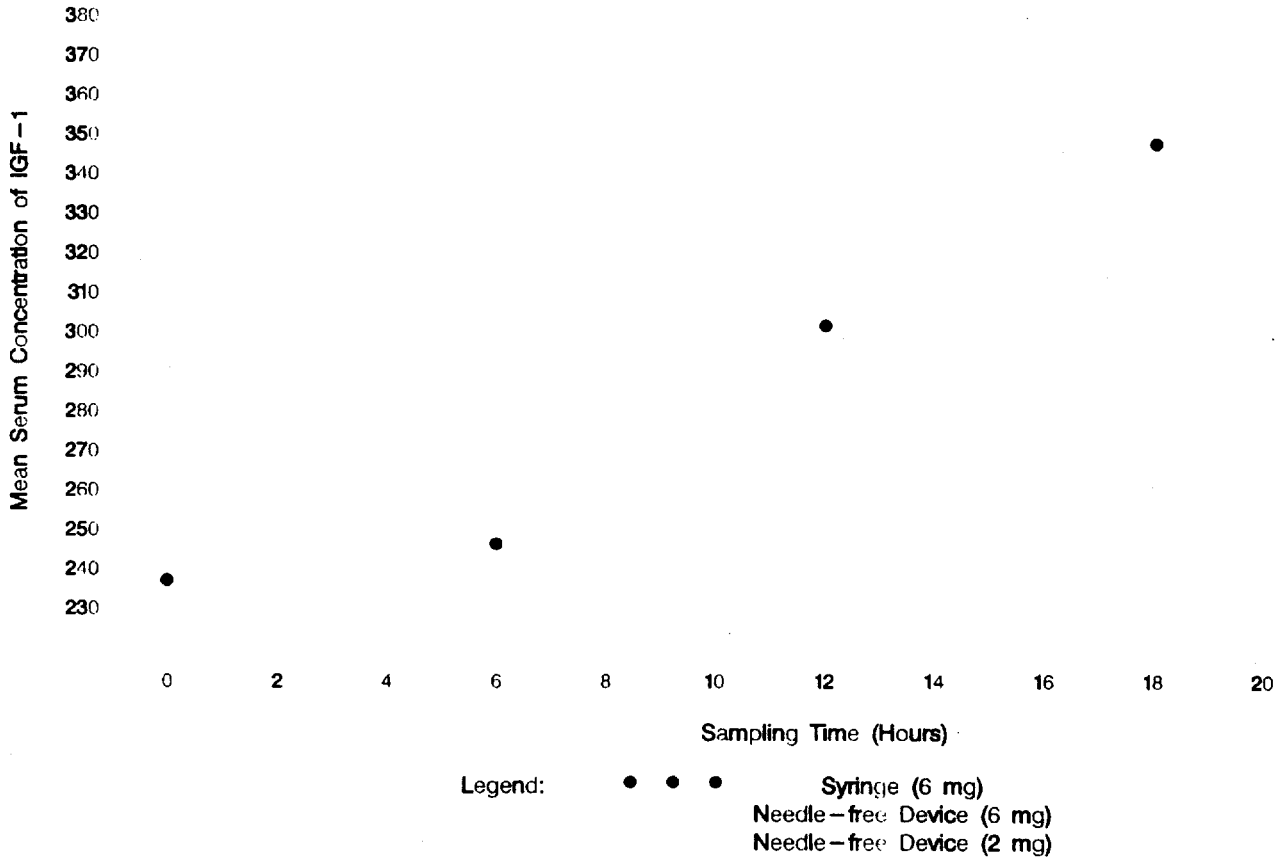
In the marketing questionnaires subjects were asked to report the sensations experienced with the two types of injections and to rate their preference between the two types. No distinctions were made in the questionnaire between the two dose formulations within the Needle-free system. No statistically significant differences were found between the Syringe and the Needle-free system. The difference in the proportion of subjects who experienced pain sensation was not significant

Concerning preference for the two injection systems, no statistically significant difference was found between the proportions of subjects preferring either system based on ease of use, convenience, less anxiety, less pain or overall preference. A higher proportion of subjects preferred the Needle-free system (69.6%) to the Syringe (30.4%) based on ease of use and convenience (69.6% for the Needle-free and 30.4% for the Syringe) ($p=0.0606$ for both comparison) although not statistically significant, pointing to a trend favoring the Needle-free system.

There was one serious adverse event in this study (acute epiglottis) which required hospitalization but unrelated to the drug or device. One subject withdrew prematurely from the study for personal family reasons and three subjects were dropped from the study as a result of wet injections as per the protocol. . The mild adverse reactions that were reported did not appear to be device related.

See Attachment # 2

Figure 2


Mean Serum Concentration of IGF-1
380
370
360
350
340
330
320
310
300
290
280
270
260
250
240
230
0
2
4
6
8
10
12
14
16
18
20
Sampling Time (Hours)
Legend:
Syringe (6 mg)
Needle-free Device (6 mg)
Needle-free Device (2 mg)

Final Clinical report Randomized Multi-Dose, three-way Crossover Relative Bioavailability and Dose Proportionality Study of Serostim®

This report summarizes the conduct of Protocol IMP 22391, including the protocol specifications, protocol compliance, adverse events, and study events. A total of 31 subjects, 17 males and 14 females, were enrolled in the study, and 26 subjects, 14 males and 12 females, completed the study. All subjects enrolled in the study satisfied the inclusion/exclusion criteria as listed in the protocol. The subjects were screened within 14 days prior to study enrollment. The screening procedure included medical history, physical examination (height, weight, Body Mass Index (BMI), vital signs, and ECG), and clinical laboratory tests (hematology, serum chemistry, urinalysis, HIV antibody screen, serum pregnancy [females only], and a screen for cannabinoids) During the study, the subjects were to remain in bed or sitting for 16 hours after the study drug was administered. Water was restricted 1 hour predose to 1 hour postdose. Food was restricted 10 hours predose to 2 hours postdose. During the study, the subjects were not allowed to engage in any strenuous activity. Sitting vital signs (blood pressure and pulse) were assessed each morning prior to dosing and at approximately 0.25, 0.50, 0.75, 1, 4, 7, 10, 13, and 16 hours postdose. A clinical laboratory evaluation (hematology, chemistries, and urinalysis) was performed at the completion of the study. Subjects were instructed to inform the study physician and/or nurses of any adverse events that occurred during the study. There were 5 subjects who were discontinued/withdrawn from the study. Subject 1003 discontinued in Period 1 due to personal reasons, Subjects 1013, 2002 and 2004 were discontinued in Period 1 and 2 due to wet injections as required by protocol, and Subject 1002 was hospitalized for acute epiglottis after completing periods 1,2, and the first 12 hours of Period 3.

There was one serious adverse event that occurred during the conduct of the study. Subject 1002 was experiencing a sore throat at the start of Period 3. The sore throat became progressively worse. The subject was monitored and his temperature was taken on a regular basis. The subject's temperature rose to 102.4°F. The Principal Investigator was consulted and requested that the subject be taken to the emergency room at Bryan LGH West Hospital, Lincoln, Nebraska. The subject was diagnosed with epiglottis and admitted to the hospital on 21 October 2000. The subject was discharged on 25 October 2000 with a prescription of Ceftin® 250-mg tablets and Tylenol® #3 capsules.

On 23 October 2000, Subject 2006 notified MDS Harris that she had confirmation from her physician that she was pregnant. The subject stated that she was using a condom with spermicide on her Medical History for birth control as required per the protocol.

A complete listing of all adverse events occurring during the study may be found in Appendix 5.4. Of Attachment #1.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR 1 3 2001

Ms. Nancy J. Gertlar
Director of QA/RA
BioJect, Incorporated
7620 Southwest Bridgeport Road
Portland, Oregon 97224

Re: K003908
Trade/Device Name: SeroJet™
Regulation Number: 880.5430
Regulatory Class: II
Product Code: KZE
Dated: December 15, 2001
Received: December 19,2001

Dear Ms. Gertlar:

This letter corrects our substantially equivalent letter of March 8, 2001 regarding the indications for use.

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent [(for the indications for use stated in the enclosure)] to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval) it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General (QS) regulation (21 CFR Part 820) and that, through periodic QS inspections, FDA will verify such assumptions. Failure to comply with the GMP regulation may result in

regulatory action. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

This letter will allow you to continue marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4692. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at their toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html".

Sincerely yours,

Patricia Cucinotta for

Timothy A. Ulatowski
Director
Division of Dental, Infection Control
and General Hospital Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): new submission

Device Name: SeroJet™

Indications for Use:

- This product is indicated for use with Serostim® [somatropin (rDNAorigin) for injection] for the treatment of AIDS wasting or cachexia.

Contraindications:

This product is not recommended for patients:

- Who are visually impaired,
- Who have neuromuscular or arthritic conditions which would make winding the SeroJet™ difficult,
- Who are not able to understand and follow the procedure for safe use of the device,
- Who bruise or bleed easily, or are taking anti-coagulant medication (blood thinners), or any other medication or therapy which may contribute to excess bleeding or bruising after injections,
- Who are not willing to fully comply with the procedures of use of the device and with the recommended frequency for replacement of the disposable accessories,
- Where Serostim® [somatropin (rDNAorigin) for injection] is contraindicated for treatment of that patient.

(PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Dental, Infection Control,
and General Hospital Devices
510(k) Number K060908

Prescription Use ✓ OR Over-The-Counter Use ____
(Per 21 CFR 801.109)